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May 24, 2002

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on SOCMA's HPV Test Plan for Benzotriazoles

Dear Administrator Whitman:

The following comments on the Synthetic Organic Chemical Manufacturers Association's (SOCMA's) test plan for benzotriazoles are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than nine million Americans.

SOCMA's category is very reasonable and straightforward, as the compounds only differ by a methyl substitution or a sodium atom. Benzotriazole and its derivatives comprise a class of corrosion inhibitors, typically used as trace additives in industrial chemical mixtures such as coolants, de-icers, surface coatings, cutting fluids, and hydraulic fluids. SOCMA has proposed to conduct one developmental toxicity test to meet the objectives of the HPV program. This test would kill 960 animals.

We would like to note SOCMA's request for Toxic Substances Control Act (TSCA) Section 4 rulemaking. As should be the case when any new testing is requested, the EPA should adhere to proper rulemaking procedure under TSCA to ensure that the proposed tests are appropriate based on what is known about potential risks and exposures and to provide for adequate scientific peer review and public input.

Many acute, sub-chronic, mutagenicity, and chronic toxicity tests have been conducted with benzotriazole, including National Toxicology Program two-year rat and mice bioassays. In the two-year carcinogenicity bioassays of 1H-benzotriazole conducted in male and female rats and mice, tumors were observed, but considered equivocal evidence of carcinogenicity.[1]

Many tests have already been conducted on animals, and additional tests will not provide definitive information on the potential developmental risks of these chemicals. Because none of the tests has been validated for their reliability or relevance to humans, we do not believe they will be useful or appropriate for providing reliable information on the developmental toxicity of the benzotriazoles.

The Mouse Embryonic Stem Cell Test for embryotoxicity has been completely validated by the European Centre

for the Validation of Alternative Methods. We recommend that the EPA immediately look into incorporating this test into the developmental toxicity test guidelines to reduce the use of animals for evaluating this endpoint.

One promising nonanimal method that is currently undergoing pre-validation is the MULTICASE-ES Trans-Species Teratogenicity model. This model is being evaluated by the Food and Drug Administration (FDA). It has been programmed with the results of more than 120,000 human studies, as well as over 10,000 studies in other animal species. A 106 compound FDA pre-validation study found the model's specificity and predictivity to be 89.7 percent and 83.3 percent, respectively, while the sensitivity was approximately 63 percent. Since this model has interagency applicability, the EPA should coordinate with the FDA and give this method, as well as other nonanimal methods for assessing developmental toxicity, priority attention.

Thank you for the opportunity to comment. I look forward to your response on this important issue. I can be reached at 202-686-2210, ext. 302, or at *ncardello@pcrm.org*. Correspondence can be sent to my attention to PCRM, 5100 Wisconsin Ave., N.W., Suite 400, Washington, DC 20016.

Sincerely,

Nicole Cardello, M.H.S.

1. National Toxicology Program. TR-88 Bioassay of 1H-Benzotriazole for Possible Carcinogenicity. 1978. *http://ntp-server.niehs.nih.gov/hydocs/LT-studies/TR088.html*